10

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Book 10

Research & Computation Dairy

This book begun November 1968

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Space for Recap of Earlier Books

Busy Work disposed of

5/6/68 – 5/9/68

previous week { Willis ✓, Eccles ✓, Ezra ✓, Gordon Shepherd ✓ }

Wrote ✓ Annual Report

letters to ✓ Per Anderson (Oslo meeting)

✓ Prof. Schenk (Buffalo Chair)

✓ Al Ochs (inquiry re retina)

✓ Rudomin (Mexico city, manuscript)

✓ J. Theod Bool – ~~notify~~ to referee paper

✓ Billy Poffenberger

✓ Rosenblith (~~Bu~~ H. Biophys Cong dates)

✓ Steven Goldstein (U. Chicago Med. Student)

✓ McIntyre

✓ Iggo

✓ Talked with MacLean & collaborator

5/13/68 Talked with Peter Gouras on P potential

Danielli ✓ 6/7/68

P.S. ... at least.

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Write

MacGregor ✓ 5/27/68

Nastuk ✓ 6/6/68

Willis ✓ 5/28/68

Burke ✓ 5/28/68

Spealman ✓ 6/13/68

Rudomin ✓ 6/6/68

?
Phone F. O. Schmitt ✓

✓ Phone Reese & Gouras

Phone MacLean ✓

✓ Phone Phil re Rudomin Symposium

Danielli ✓ 6/7/68

Checklist June 17–21

Write MacGregor ✓
Snell ✓
Schmitt ✓
MacKay ✓
Laibovie ✓
Science ✓
Miss Leslie ✓
Brookhart ✓
Gordon Shepherd ✓

Phone MacLean ✓
Write Nomination for John Evans ✓
~~Write Eccles~~ ✓
Ask Dorothy for travel order ✓

Look up Binghampton ✓

July 3, 1968 Checklist

Write Gordon ✓
Write Scheibels ✓
Write John Evans' nomination
Register for Intl. Congress ✓
~~Congress Invitations~~ ✓
Order N.Y. Acad. reprints (find letter quotation)

Order Cajál

Equalizing Time Constants

Sometime, note to Exp. Neurol. with Mannen

also — Aitken & Shepherd

July 15, 1968

Today I spent the day adding halfway down to finite cylinder series solutions.

Before Friday must

Authorize check deposits
Write MacKay
? Write Leibovic
? Work on Equalizing time constants.
John Evans nomination
Lerner "
Send manuscript to Lerner

7/16/68

Took care of

✓ Lanier Manuscript with covering letter
✓ Leibovic note
✓ NRP nomination for John Evans
✓ note to " "
✓ NPP nomination for Lanier

Still need to write MacKay
✓ & write Tsukahara

August 19, 1968

Professor D. M. MacKay
University of Keele

Dear Donald,

Please excuse my delayed reply. I have just returned from a much needed vacation; the first really relaxed one in several years. Today I am picking up the threads and returning to the busy life. To expedite it, I am typing this letter myself.

I shall be happy to participate in your work session and will plan to be ready with 10-15 minutes of introductory material on Monday morning. Your letter did not include your introductory program as an enclosure; consequently, I have not yet seen your outline.

Although I shall have to think a little more about exactly what to say, what I have in mind just now can be summarized as follows:

1. I am not an authority on evoked potentials in all their variety, but,

2. my experience encourages me to believe that it is possible to compute and thus predict the extracellular potentials generated by specified sequences of activity in specified populations of neurons;

3. such computations are simplest when the subpopulations of neurons are characterized by synchronous activity and by symmetric geometry, but

4. specified asynchrony and specified asymmetry could be provided for in more complicated computations.

5. The inverse problem, of inferring geometry and sequence of activity from the resultant extracellular potentials is much more difficult; in general, it has no unique solution.

6. Only by means of much auxiliary information on the underlying geometry and possible sequences of activity, would it seem feasible to seek valid solutions to this inverse problem.

Did you have in mind that I should give explicit details of the olfactory bulb study to ~~[illegible]~~ illustrate my approach, or would you prefer to have those details deferred to a later point in the program?

Sincerely

P.S. I plan to remain in Brookline until Tuesday noon, at least.

11/8/68 – Recap

Regular notetaking was suspended for almost a year. Things have been rather hectic.

Note: Ravello in May & June 1967
Keele in September 1967 p.172 book 9
Udo's retinal detachment " < Caianiello manuscript
NRP Coding in Jan 1968 also explorations with John Evans
Atlantic City Symposium April 1968
* Completion of O'Bulb Manuscript (Feb & Mar 1968)
Invitation from Oslo
Job offer from Buffalo 5/9/68
Journal of P potential 5/14/68
Refereeing of MacGregor Rand Report
Rudomin informal referee of others
Bob Burke inquired about equalizing τ 5/28/68
Beach in July
Intl. Physiol Congress in August
Working on equaliz τ manuscript in Sept.
Julian Jack visit in early October
Gave him 1st 15 pages of xerox draft
He has not used equalizing τ
He used image method (reflections) for matching B.C.
Also Johannesma on Sept. 25
Sept 16 – J. Neurophysiol galley proofs
Also in Sept – Talked with Phil, Bob + Dieter Lux
They decided not to go into complications that I detailed in memo & computed ↑ 9/4/68
AC admittance & phase angle

11/8/68 recap

*

Also 9/6/68 – 9/10/68 wrote ~~& test~~ WR68IT using remote station for real & imag. parts for inf. cyl, finite cyl, & various ρ.

Then, for two weeks of October, pressed on with equalizing τ manuscript.

FLU Missed NRP ~~Evoked Po~~ (Mackay) Oct 20–22
" Buffalo – had already declined
Went to Mohawk Meeting Oct 27–30
Refereeing Oct 17–25
Letter from Fessard re IBRO Central Council

1st week of November 1968:
More refereeing – resolved no more for a while
Trying to work out arrangements for
IBRO – Paris Dec. 16
Scheibels – LA Feb 20
Cowan here March ~~18~~ 26
Boulder – July 21 – Aug 8
Rockefeller – Jan 9
Oslo – Sept 15–17
must keep lid on

Planning to resume & polish off equalizing τ
(a) Still need to complete part with ρ
(b) and several dendrites allowing for different length –
(c) Then, probably separate eigenvalue part from complete solution part

11/8/68

Today, before resuming work on equalizing & manuscript, thought about the problem that I had been considering for the Goldstein or Levine work on. Solved crux here.

From N.Y. Acad paper when $K \neq 0$

PDE $$\frac{\partial^2 V}{\partial Z^2} + K\frac{\partial V}{\partial Z} = V + \frac{\partial V}{\partial T}$$

St.St. $$\frac{d^2V}{dZ^2} + K\frac{dV}{dZ} - V = 0$$

$(s+a)(s-b)$ $$(s^2 + Ks - 1)v = 0$$

$-ab = -1$

$a - b = K$

$$V(Z) = Ae^{-aZ} + Be^{+bZ}$$

$r_1 = -a$ where $a = \frac{K + \sqrt{K^2+4}}{2} = 1 + \epsilon$ something small if K is small +

$r_2 = +b$ $-b = \frac{K - \sqrt{K^2+4}}{2} = -1 + \epsilon$ something small if K is small +

(note: for $K > 0$, $a > b > 0$ because $-ab = -1$ and $a - b = K$)

Separation of variables for transient.

$$V(Z,T) = U(Z)\,e^{-(1+\gamma^2)T}$$

Subst in PDE
$$\left(\frac{d^2U}{dZ^2} + K\frac{dU}{dZ}\right)e^{-(1+\gamma^2)T} = (1 - 1 - \gamma^2)e^{-(1+\gamma^2)T}$$

$$\therefore \frac{d^2U}{dZ^2} + K\frac{dU}{dZ} + \gamma^2 U = 0$$

$$(s^2 + Ks + \gamma^2)u = 0$$

Can show we only want roots for $\gamma = 0$ and $\gamma^2 > K^2/4$

Here $U(z) = Ae^{-\alpha z} + Be^{-\alpha^* z}$ (α^* → β)

where α & α^* (α^* → β) are complex conjugates defined by

$$\alpha = \frac{K \pm \sqrt{K^2 - 4\gamma^2}}{2}$$

Note $\alpha\beta = \gamma^2$, $\alpha + \beta = K$

Notice, if $\gamma = 0$, this is case of uniform decay for both ends sealed. roots are zero & K

Zero root fits uniform decay e^0

But e^{-KZ} can be excluded as unable to satisfy the two sealed end B.C.

Similarly $0 < \gamma < \sqrt{K^2/4}$ gives real roots which cannot satisfy two sealed ends.

Because $\frac{dU}{dZ} = -\alpha A e^{-\alpha Z} - \beta B e^{-\beta Z}$

set zero at $Z = 0$ gives $\alpha A = -\beta B$

and at $Z = L$ need $e^{-\alpha L} = e^{-\beta L}$

which is not possible for real $\alpha \neq \beta$

But it is possible when α & β are complex

$$\alpha = \frac{K}{2} \pm i\sqrt{\gamma^2 - K^2/4} \quad \text{for } \gamma^2 > K^2/4$$

let $\theta_n = \sqrt{\gamma_n^2 - K^2/4}$

or $\gamma_n^2 = \theta_n^2 + \frac{K^2}{4}$

from bottom right

Note that $\begin{cases} n = 0 \\ \theta = 0 \end{cases}$ would solve B.C. at $Z = L$
but not B.C. at $Z = 0$

however, can have $\sin \theta L \neq 0$
provided that
$$\frac{-KB}{2} - \theta A = 0$$

implying $\frac{B}{A} = -\frac{2\theta}{K}$

But BC at $Z=0$ already gave $\frac{B}{A} = \frac{K}{2\theta}$

This would require $\frac{K}{2\theta} = -\frac{2\theta}{K}$
$$4\theta^2 = -K^2$$
or $\boxed{\theta = i K/2}$ or $\frac{B}{A} = -i$

But, if put this in top line of p. 12, get
$$e^{-KZ/2}\left\{C_1 e^{-KZ/2} + C_2 e^{+KZ/2}\right\}$$
$$= C_1 e^{-KZ} + C_2 e^{0}$$

where B.C. require $C_1 = 0$
& leave C_2 arbitrary

with $\theta = i K/2$
$\theta^2 = -\frac{K^2}{4}$
$\gamma^2 = 0$

Now, for these complex roots, we write

$$U(Z) = e^{-KZ/2}\{C_1 e^{+i\theta Z} + C_2 e^{-i\theta Z}\}$$

$$= e^{-KZ/2}\{A\cos\theta Z + B\sin\theta Z\}$$

$$\frac{dU}{dZ} = e^{-KZ/2}\left[\left(-\frac{KA}{2} + \theta B\right)\cos\theta Z + \left(-\frac{KB}{2} - \theta A\right)\sin\theta Z\right]$$

$$\frac{d^2U}{dZ^2} = e^{-KZ/2}\left[\left(\frac{K^2A}{4} - K\theta B - \theta^2 A\right)\cos\theta Z + \left(\frac{K^2B}{4} + K\theta A - \theta^2 B\right)\sin\theta Z\right]$$

Testing this solution in $\left(\frac{d^2}{dZ^2} + K\frac{d}{dZ} + \gamma^2\right)U = 0$

Coeff of $\cos\theta Z$ is $e^{-KZ/2}\left[\frac{K^2A}{4} - K\theta B - \theta^2 A - \frac{K^2A}{2} + K\theta B + \gamma^2 A\right]$

or zero

$$\downarrow$$
$$\theta^2 A + \frac{K^2A}{4}$$

Similarly for coeff of $\sin\theta Z$ get

$$e^{-KZ/2}\left[\frac{K^2B}{4} + K\theta A - \theta^2 B - \frac{K^2B}{2} - K\theta A + \gamma^2 B\right]$$

$$\downarrow$$
$$\theta^2 B + \frac{K^2B}{4}$$

QED or zero QED

$\frac{dU}{dZ} = 0$ at $Z = 0$ gives $0 = 1\left[\left(-\frac{KA}{2} + \theta B\right)\times 1 + 0\right]$

$$\therefore \frac{B}{A} = \frac{K}{2\theta} = \frac{KL}{2n\pi}$$

& at $Z = L$

$$0 = e^{-KL/2}\left[(0)\cos\theta L + \left(-\frac{KB}{2} - \theta A\right)\sin\theta L\right]$$

$\therefore \sin\theta L = 0$

See left

$\theta L = n\pi \qquad \theta_n = n\pi/L$

e.g. $K=1$, $L=1$, $e^{KL}=2.718$ for $\frac{n}{n_0}$

$e^{-KL/2}=0.606$

$e^{-KL/4}=0.779$

$n=1$, $\frac{KL}{2n\pi}=\frac{1}{6.28}$, $\tau_0/\tau_1 = 1 + .25 + 9.87 = 11.12$

$n=2$, $\frac{KL}{2n\pi}=\frac{1}{12.56}$, $\tau_0/\tau_1 = 1. + .25 + 39.6 = 40.85$

Note sine term makes max contribution for $Z = L/2$

Therefore, for two sealed ends, we find that for each n there is a term in $U(Z)$

$$A_n e^{-KZ/2}\left\{\cos(n\pi Z/L) + \frac{KL}{2n\pi}\sin(n\pi Z/L)\right\}$$

also, note $\theta_n^2 = \frac{n^2\pi^2}{L^2} = \gamma_n^2 - \frac{K^2}{4}$

or $\gamma_n^2 = \frac{n^2\pi^2}{L^2} + \frac{K^2}{4}$

∴ The solution can now be written

for $\frac{\partial^2 V}{\partial Z^2} + K\frac{\partial V}{\partial Z} = V + \frac{\partial V}{\partial T}$

for both ends sealed

of arbitrary initial condition

$$V(Z,T) = A_0 e^{-T} + e^{-KZ/2}\sum_{n=1}^{\infty} A_n \left\{\cos(n\pi Z/L) + \frac{KL}{2n\pi}\sin(n\pi Z/L)\right\} e^{-\left(1+\frac{K^2}{4}+\frac{n^2\pi^2}{L^2}\right)T}$$

where the effect of $K \neq 0$ can be seen at three points ◎ & of course also would affect an initial steady state with current or voltage clamp.

Further problems: (1) other B.C.

(2) various I.C.

(3) two or more regions, e.g.

+/or E+I.

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Therefore, for ~~two sealed ends~~ $K \neq 0$ we find that, e.g. for each m there is a term in $V(Z)$

$$A_m e^{-KZ/2}\left\{\cos(m\pi Z/L) + \frac{KL}{2m\pi}\sin(m\pi Z/L)\right\}$$

$e^{-K/2} = 0.606$

$$\alpha_m^2 = \frac{m^2\pi^2}{L^2} = \gamma_m^2 - \frac{K^2}{4}$$

$m=1, \quad \frac{KL}{2m\pi} = \frac{1}{2\pi}$ [illegible] $\gamma_1^2 = 1 +$ [illegible] $= 11.12$

or $\gamma_m^2 = \frac{m^2\pi^2}{L^2} + \frac{K^2}{4}$

$m=2$, [illegible] $+ .25 + 39.6 = 40.85$

Note [illegible] contribution for Z [illegible]

∴ The solution can now be written

for $\frac{\partial^2 V}{\partial Z^2} + K\frac{\partial V}{\partial Z} = V + \frac{\partial V}{\partial T}$

for both ends sealed & arbitrary initial condition

$$V(Z,T) = A_0 e^{-T} + e^{-KZ/2}\sum_{m=1}^{\infty} A_m\left\{\cos(m\pi Z/L) + \frac{KL}{2m\pi}\sin(m\pi Z/L)\right\} e^{-\left(1+\frac{K^2}{4}+\frac{m^2\pi^2}{L^2}\right)T}$$

where the effect of $K \neq 0$ can be seen at three points ◯. + of course also would effect an initial steady state with current or voltage clamp.

Further problems: (1) other B.C.

(2) various I.C.

(3) two or more regions, e.g. for E + Y

11/27/68 day before Thanksgiving

Have just spent several days thinking about & preparing a statement on the "Role of Mathematical Theory in the Neurosciences". This prompted by plans of NRC Committee on Brain Sciences to discuss the scope of neurosciences in the light of a draft report (by Kuffler et al) which makes no reference at all to mathematical or biophysical theory.

During this same time, of course, I wrote Oxford & was making arrangements for Paris trip. Also worked up three more pages of equalizing E manuscript, and did other odd chores. Yesterday, got request from Science to review Proceedings of 4th Intl. Meeting of Neurobiologists (Stockholm 66) entitled "Structure and Function of Inhibitory Neural Mechanisms". This is the one where Bob Burke presented his data & Eccles dropped his old position. Tremendous number of items — big chore to review. Feel entitled to decline because of NRC & IBRO, as well as personal involvement with Burke-Eccles issue.

Gordon Shepherd invited by Eccles to write review.

Musing about Reviews, textbooks, monographs.

The first book I should aim at should be

~~"Introduction to Theoretical Neurophysiology"~~ Experimental Theory of Neurons

With emphasis on [physiol → physics → math] building up intuitive grasp of this interrelation with the simplest examples. (over)

Also note that a comprehensive & eclectic treatise would best be prepared by someone who has conscientiously taught such material to students in courses for several years. I have not. My effort has been devoted mainly to individual research, with occasional lecturing & teaching.

∴ Personal approach is natural & more or less unavoidable

11/27/68 Thoughts about

(Experimental Neuron Theory)

Introduction to Theoretical Neurophysiology

Preface emphasizing personal approach
belief in building intuitive grasp of
physical → physics → math

with simplest examples first.
Then move on to more complicated cases
& to general solutions.

~~Part I — Passive nerve membrane~~
~~A. lumped patch~~
~~(1) intuitive approach, steady state as a potential divider $V = \frac{G_r}{G_r+G}$~~ comes later
~~B. ~~cylinder~~ infinite cylinder in medium of zero~~

~~Chap~~ Part I — Lumped patch of membrane
A — passive
B — synaptic   1st pot. divider idea, then full math
C — active

~~Chap~~ Part II — Nerve Cylinders ~~[illegible]~~ steady states
A — infinite length
B — finite length
C — Soma dendrites

~~Chap~~ Part III — Transients in cylinders of infinite leng
~~Chap~~ Part IV — Transients in cylinders of finite length

Chapt V – Transients in Neurons

Could defer to a separate volume:

Chapt VI – Extracellular field of spherical cell

Chapt VII – Extracellular field of cylinders

Chapt VIII – Extracell field of soma + dendrite

Chapt IX – Extracell field of pop. of neurons

Chap ~~X~~ – Spatio-temporal synaptic patterns

maybe earlier

Chapt ~~XI~~ – Interacting neurons

Avoid compulsion to include everything.

Emphasize understanding of the simpler cases.

State more complicated cases & refer to literature

Footnote: ~~If readers~~ Those readers who would like to see additional details included in a second edition are invited to write the author or the publisher specifying points where need is felt.

1/15/69 Thurs.
(Last week at Rockefeller University)

Also, last week, started Steven Goldstein on problem from NY Acad. reprint — See p. 8 of this notebook. He worked out most of the same results independently.

This week, confronted with problem of non-orthog.

i.e. our eigenfunctions are A_0

and $A_n e^{-KZ/2} \sum \left\{ \cos n\pi Z/L + \frac{KL}{2n\pi} \sin \frac{n\pi Z}{L} \right\}$

But, these eigenfunctions are not orthogonal.

At first, I thought of Churchill's paper which Jim had used to solve my earlier problem, but that was a boundary condition difficulty; furthermore, that general class does not include the present problem.

So we consulted Jim again

He pointed out two important things

(1) the factor $e^{-KZ/2}$ can be factored out because it does not depend upon n

(2) Our PDE separated to ordinary DE is not self adjoint, but it can be converted to self adjoint form as reviewed on next page.

{Self-Adjoint operators / Sturm-Liouville Equations}

Cf Margenau & Murphy pp 253–255

Churchill (Fourier Series & BVP) p. 47 & p. 49

Ince p. 215

Agnew – pp 251–277 esp p. 257

~~The general differential equation~~

~~$p_0(x)\frac{d^2y}{dx^2} + p_2(x)\frac{dy}{dx} + [f_2$~~ From Ince

The general homogeneous linear differential operator of 2nd order

$$L(u) = p_0 \frac{d^2u}{dx^2} + p_1 \frac{du}{dx} + p_2 u$$ (where $p_n(x)$ are fns of x)

is not self-adjoint in general, but it is self-adjoint if

$$p_0' = p_1$$

Then $L(u) \equiv \frac{d}{dx}\left(p_0 \frac{du}{dx}\right) + p_2 u$

which is the operator studied by Sturm & Sturm-Liouville

* We can use the factor $\frac{c}{p_0} e^{\int \frac{p_1}{p_0} dx}$ to form a self adjoint operator

i.e. $$\frac{c}{p_0} e^{\int \frac{p_1}{p_0} dx} L(u) \equiv \frac{d}{dx}\left\{e^{\int \frac{p_1}{p_0} dx} \frac{du}{dx}\right\} + \frac{p_2}{p_0} e^{\int \frac{p_1}{p_0} dx} u$$

where C is a constant to be chosen

If U_n & U_m are distinct eigenfunctions →

$$\int_a^b p(x)\, U_n U_m \, dx = 0$$ is the orthogonality relation

Whereas $$\int_a^b U_n U_m \neq 0$$

yet Churchill does call this orthogonality of U_n & U_m

one could regard $(\sqrt{p}\, U_n)(\sqrt{p}\, U_m)$ as the orthogonal fcns.

Note, since $U_0 = A_0$, this means also that

$$\int_0^L e^{KX} U_n \, dx = 0$$

$$A_n \int_0^L e^{+KX/2} \left\{ \cos\left(\frac{n\pi x}{L}\right) + \frac{KL}{2n\pi} \sin\left(\frac{n\pi x}{L}\right) \right\} dx = 0$$

More specifically, from Churchill p. 47

Given $u'' + f_1(x)\, u' + \{f_2(x) + \lambda f_3(x)\} u = 0$

use factor $r(x) = e^{\int f_1(x)\,dx}$ weighting or $w(x)$ factor

to form $\frac{d}{dx}\left[r(x)\frac{du}{dx}\right] + \{q(x) + \lambda p(x)\} u = 0$

which is a Sturm-Liouville equation

where $q(x) = r(x) f_2(x)$

$p(x) = r(x) f_3(x)$

In present problem $u'' + K u' + \lambda u = 0$ $\lambda = \gamma^2$

$\therefore r(x) = e^{\int K dx} = e^{Kx}$

$\therefore \frac{d}{dx}\left[e^{Kx}\frac{du}{dx}\right] + \lambda e^{Kx} u = 0$

$\therefore p(x) = e^{Kx}$

$\therefore$ we have that

← $\int_0^L e^{Kx}\, u_n u_m\, dx = 0$

$A_n A_m \int_0^L \left[\left\{\cos\left(\frac{n\pi x}{L}\right) + \frac{KL}{2n\pi}\sin\left(\frac{n\pi x}{L}\right)\right\}\left\{\cos\left(\frac{m\pi x}{L}\right) + \frac{KL}{2m\pi}\sin\left(\frac{m\pi x}{L}\right)\right\}\right] dx$

$= 0$

Change on cond[illegible] dist[illegible]

On physical grounds

Apalogoday found for cylinder

A_0 is average of $f(z)$ over interval, weighted for surface area

i.e. $$\frac{\int_0^L f(z)\frac{dA}{dz}\,dz}{\int_0^L \frac{dA}{dz}\,dz}$$ where dA is increment in surface area.

$$\frac{dA}{dx} = 2\pi r n$$

$$\frac{dA}{dz} = 2\pi r n \frac{dx}{dz}$$ & $\frac{dx}{dz} \propto r^{1/2}$

$$\propto 2\pi r n^{3/2}$$

$$\propto e^{kz}$$ → p. 1079 of NY. Acad. because we here take $\frac{ds}{dx} = 1$

would[illegible] apply for more general $\frac{ds}{dx}$

$$\therefore A_0 = \frac{\int_0^L f(z)e^{kz}\,dz}{\int_0^L e^{kz}\,dz}$$

1/15/69 continued   Now

$$f(x) = A_0 + \sum_{n=1}^{\infty} A_n e^{-Kx/2}\left\{\cos\left(\frac{n\pi x}{L}\right) + \frac{KL}{2n\pi}\sin\left(\frac{n\pi x}{L}\right)\right\}$$

$$e^{Kx} f(x) = e^{Kx} A_0 + \sum_{n=1}^{\infty} A_n e^{+Kx/2}\left\{\cos\left(\frac{n\pi x}{L}\right) + \frac{KL}{2n\pi}\sin\left(\frac{n\pi x}{L}\right)\right\}$$

Integrate each term ~~from~~ over interval,

get $\int_0^L e^{Kx} f(x)\,dx = A_0 \int_0^L e^{Kx}\,dx + 0$ for each term of series

↑ see bottom p. 25

$$\therefore A_0 = \frac{\int_0^L f(x)\, e^{Kx}\,dx}{\int_0^L e^{Kx}\,dx}$$

as was already deduced on physical grounds

see left.

Here x corresp to z of NY acad problem

Also

$$A_n = \frac{\int_0^L f(x)\, e^{+Kx/2}\left\{\cos\left(\frac{n\pi x}{L}\right) + \frac{KL}{2n\pi}\sin\left(\frac{n\pi x}{L}\right)\right\}dx}{\int_0^L \left\{\cos\left(\frac{n\pi x}{L}\right) + \frac{KL}{2n\pi}\sin\left(\frac{n\pi x}{L}\right)\right\}^2 dx}$$

1/16/69

Because
$$\int e^{ax}\cos px\,dx = \frac{e^{ax}(a\cos px + p\sin px)}{a^2+p^2}$$
$$\int e^{ax}\sin px\,dx = \frac{e^{ax}(a\sin px - p\cos px)}{a^2+p^2}$$

See p. 309 of 12th ed. of CRC math Table.

It follows that
$$\int_0^L e^{Kx/2}\left\{\cos n\pi x/L + \frac{KL}{2n\pi}\sin n\pi x/L\right\}dx =$$
$$\left[\frac{e^{Kx/2}}{\left(\frac{K}{2}\right)^2+\left(\frac{n\pi}{L}\right)^2}\left(\frac{K}{2}\cos\frac{n\pi x}{L} + \frac{n\pi}{L}\sin\frac{n\pi x}{L} + \frac{K^2 L}{4n\pi}\sin\frac{n\pi x}{L} - \frac{n\pi}{L}\frac{KL}{2n\pi}\cos\frac{n\pi x}{L}\right)\right]_0^L$$
$$= 0$$

Now denominator of A_n

$$\int_0^L\left\{\cos\left(\frac{n\pi x}{L}\right) + \frac{KL}{2n\pi}\sin\left(\frac{n\pi x}{L}\right)\right\}^2 dx =$$

$(\cos a + b\sin a)^2 = \cos^2 a + 2b\cos a\sin a + b^2\sin^2 a$

$a = \frac{n\pi x}{L}$
$b = \frac{KL}{2n\pi}$

$$\frac{L}{n\pi}\left[\frac{1}{2}\sin a\cos a + \frac{a}{2} + b\sin^2 a - \frac{b^2}{2}\cos a\sin a + \frac{b^2 a}{2}\right]$$
$$= \frac{L}{n\pi}\left(0-0+\frac{n\pi}{2} - 0 + 0 - 0 + 0 - 0 + \left(\frac{KL}{2n\pi}\right)^2\frac{n\pi}{2}\right)$$
$$= \frac{L}{2}\left(1+\left(\frac{KL}{2n\pi}\right)^2\right) \quad \text{or} \quad \left(\frac{n\pi}{2} + \frac{(KL)^2}{8n\pi}\right)\frac{L}{2}$$

?

for $C_n = 2C_0(-1)^n$ for δ input at $\frac{\pi}{L}=2$ [illegible]

$$G(t_p) = \frac{2\left[1+4\left(\frac{\pi}{L}\right)^2\right]}{\left[+2\left(1+\frac{\pi}{L}\right)^2-G\right]^3} - \frac{2\left[1+9\left(\frac{\pi}{L}\right)^2\right]}{\left[+2\left(1+\frac{\pi}{L}\right)^2-G\right]^8} + \cdots$$

$$\simeq \frac{(\pi/L)^2}{\left[1+(\pi/L)^2\right]^3}$$

e.g. if $\pi/L = 2$ get $\simeq \frac{4}{125} = .03$ 3 parts per thousand in arg. of ln

compared with $2[1+4] = 10$

9.97

i.e. for this case $t_p/\tau_m = \left(\frac{1}{2}\right)^2 \ln\{10\}$

$$= \frac{2.303}{4} = 0.576$$

$$\frac{2.2996}{4} = 0.575$$

note that $e^{-(n^2-1)\left(\frac{\pi}{L}\right)^2 t_p/\tau_m} \simeq \left\{-\frac{c_1}{c_0}\left[1+\left(\frac{\pi}{L}\right)^2\right] - G(t_p)\right\}^{-(n^2-1)}$

$$\therefore G(t_p) = \sum_{n=2}^{\infty} \frac{c_n}{c_0} \frac{\left[1+\left(\frac{n\pi}{L}\right)^2\right]}{\left\{-\frac{c_1}{c_0}\left[1+\left(\frac{\pi}{L}\right)^2\right]-G\right\}^{(n^2-1)}}$$

$$\simeq \frac{c_2}{c_0} \frac{\left[1+4\left(\frac{\pi}{L}\right)^2\right]}{\left\{-\frac{c_1}{c_0}\left[1+\left(\frac{\pi}{L}\right)^2\right]\right\}^3} + \text{smaller terms}$$

Peak of decay transient

Recap & Generalize earlier result from Dec 1967

$$V(t) = C_0 e^{-k_0 t} + C_1 e^{-k_1 t} + \sum_{n=2}^{\infty} C_n e^{-k_n t}$$

$$\dot{V}(t) = -k_0 C_0 e^{-k_0 t} - k_1 C_1 e^{-k_1 t} - \sum_{n=2}^{\infty} k_n C_n e^{-k_n t}$$

When $\dot{V}(t) = 0$, $t = t_p$, and we can write (divide by $k_0 C_0 e^{-k_1 t_p}$)

$$e^{-(k_0 - k_1) t_p} = -\frac{k_1 C_1}{k_0 C_0} - \sum_{n=2}^{\infty} \frac{k_n C_n}{k_0 C_0} e^{-(k_n - k_1) t_p}$$

or ln both sides

$$(k_1 - k_0) t_p = \ln\left\{ -\frac{k_1 C_1}{k_0 C_0} - \sum_{n=2}^{\infty} \frac{k_n C_n}{k_0 C_0} e^{-(k_n - k_1) t_p} \right\}$$

Now for cylinder of electrotonic length, L, and sealed ends,

$$k_n = \left[1 + \left(\frac{n\pi}{L}\right)^2\right] k_0 = \frac{1 + \left(\frac{n\pi}{L}\right)^2}{\tau_m}$$

$$k_1 - k_0 = \left(\frac{\pi}{L}\right)^2 k_0 = \frac{(\pi/L)^2}{\tau_m} \qquad k_n - k_1 = (n^2 - 1)\left(\frac{\pi}{L}\right)^2 k_0$$

$$\frac{k_1}{k_0} = 1 + (\pi/L)^2 \qquad \frac{k_n}{k_0} = 1 + \left(\frac{n\pi}{L}\right)^2$$

$$\therefore \quad t_p/\tau_m = \left(\frac{L}{\pi}\right)^2 \ln\left\{ -\frac{C_1}{C_0}\left[1 + (\pi/L)^2\right] - G(t_p) \right\}$$

where (usually small)

$$G(t_p) = \sum_{n=2}^{\infty} \frac{C_n}{C_0}\left[1 + (n\pi/L)^2\right] e^{-(n^2-1)(\frac{\pi}{L})^2 t_p/\tau_m}$$

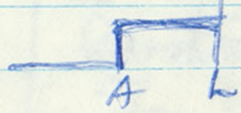
see left

Example

Now, for initial condition weighted most in outer half of cylinder, we get, for $V(t) = Z = 0$, that C_1 has opposite sign to C_0 + formula can be used as stated

Note $$\frac{C_1}{C_0} = \frac{2\int_0^L F(X)\cos\left(\frac{\pi X}{L}\right)dX}{\int_0^L F(X)\,dX}$$

for $F(x) = \delta(L-X)$, get $\frac{C_1}{C_0} = \frac{-2}{1} = -2$

for $F(x) =$ , get $\frac{C_1}{C_0} = \frac{-2\sin(\pi A/L)}{(\pi/L)(L-A)}$

for $F(x) = \delta(A-X)$, get $\frac{C_1}{C_0} = 2\cos\left(\frac{\pi A}{L}\right)$

∴ For above $$\frac{t_p}{\tau_m} \simeq \left(\frac{L}{\pi}\right)^2 \ln\left\{\frac{2\left[1+\left(\frac{\pi}{L}\right)^2\right]\int_0^L F(x)\cos\left(\frac{\pi X}{L}\right)dX}{\int_0^L F(x)\,dX}\right\}$$

for δ ⟶ $\left(\frac{L}{\pi}\right)\ln\left\{+2\left[1+\left(\frac{\pi}{L}\right)^2\right]\cos(\pi A/L)\right\}$

for  get $\left(\frac{L}{\pi}\right)\ln\left\{\frac{-2\left[1+\left(\frac{\pi}{L}\right)^2\right]\sin(\pi A/L)}{(L-A)(\pi/L)}\right\}$

Simplest is δ at L, then get $\left(\frac{L}{\pi}\right)\ln\left\{-2\left[1+\left(\frac{\pi}{L}\right)^2\right]\right\}$

2/6/69

Just spent last several weeks

ⓐ getting Steven Goldstein started
ⓑ writing final draft of equalizing τ paper
ⓒ included working out θ dependence appendix
and also voltage clamp
& multiple cylinders to one soma.

Most of it has been proofread & xeroxed today

Still need [Conclusions
Abstract
Fig. 1 & Fig legend

Papers

I — Equalizing τ
II — Explicit Solutions
III — Solutions for peaks etc.
IV — AC admittance
V — cylinder in applied external field

Also — Extracellular Potentials
with John Evans & EEG Congress
& EEG Handbook

Also — preprint for Scheibel work session

Recently refereed & also wrote help to Ill. Grad Student (Wilkens)

May 19, 1969

Last two months have been hectic
End of February included funeral (Harold Freed)
& Scheibel symposium
& visit to John Evans

first half of March devoted to chores
Rest of March, all of April & 1st half of May
devoted mainly to working out details &
writing up new paper:

Paper II [Distributions of Potential in Cylindrical
Coordinates and Time Constants for a
Membrane Cylinder.] which grew

out of what was at first an appendix of
equalizing time constant paper.

last Friday – May 16 – completed original &
5 xerox copies of what I hope is final
draft.
Copies being read by John Rinzel
Jose
Jim

Paper I Now need to do final cleanup of Equalizing
Time constant paper which was
essentially finished in February
before going to Scheibel Symposium.
When ready: Send copies to Jack & Redman.

Last week politely declined

(1) Teuber — IBRO Symposium Committee

(2) Yphantis — Biophysical Soc. Council
Nomination

May 26, 1969

Now have 8 xeroxes of corrected Paper I
5 " " " " Paper II
+ will make a few final corrections to original of II
before running off more xeroxes

Clearance copies going 5/26/69 to NIAMD Clearance today.
Should get ~~Figs~~ from Art ~~Dept~~ ~~tomorrow~~.
(↑ two for paper II.)

Paper I

original

5/23/69
- copy #1 ~~Moxes~~ mailed to Boulder } Redman
- #2 ~~Jack~~ J. Jack 7/11/69
- #3 John Evans

(include 5/26/69 corrections)
- #4 ~~Ringelt~~ carry to Boulder (Master)
- #5 desk
- #6 Hagins
- #7 Home
- #8 – Clearance

Paper II

original

5/16/69
- copy #1 ~~Ringelt~~ Redman mailed to Boulder
- #2 Zian → Clearance
- #3 ~~Jack~~ 7/11/69 J. Jack
- #4 ~~Moxes~~ John Evans
- #5 Master ~~desk~~ Corrections

5/26/69
- #6 K.S. Cole 9/25/69
- #7 desk
- #8 Hagins
- #9 Home

○ means updated 6/3/69

? Copies for Julian Jack
Stephen Redman
Steven Goldstein

Pickard
Footnotes 1 + 7
p. 41 Lorente

Made 4 more xeroxes 9/3/69 of corrected
~~Gave one to Bob Burke~~
~~Send~~ one to Oslo, brought back : one to Cole 9/25/69

○ submitted 6/4/69 ○ submitted 6/4/69
To Biophysical J.

Have been very busy

Boulder in July & August (1969)

Norway in September (1969)

Worked on Oslo manuscript after return

Handicapped by no Secretary

got overtime typing.

Bioph. J. Galley proofs came Oct 9, 1969

returned Oct 11, 1969

Finally completed Oslo manuscript typing & xeroxing

Oct 15, 1969

8 xerox copies

1 sent to Oslo with original

1 home

1 master

1 Hagins for referee

1 Burke for referee

3 in cabinet

February 24, 1970

Starting to write up dendritic spine work with John Rinzel.

Take time for a moment to go over loose notes on development.

We started talking in March or April 1969

4/11/69 John ~~wrote~~ memo on his version of compartmental calcs. for straight chain
& memo of equations & urged twig. calc.
4/31/69 John produced a few twig results.
5/8/69 my memo proposing specific computations.
5 cpts. $\Delta Z = 0.2$ plus one twig at end.
* use different values for coupling R
calc. steady state
& for ε, i & v pulses.
made qualitative predictions.
* { twig v increase with R_c increase
  soma v decrease with R_c increase }
5/9/69 some more detailed suggestions
{ John produced some computed results
  resistance ratios }
5/13/69 John's followup memo on resistance ratios

6/5/69 my memo on possible collaborative projects that could lead to publishable papers.

① Inputs to dendritic spines
② Explore Action Pot. Model
③ Use Cpt. & Act. Pot. model to compute EC Pot.
④ Small set of connected neurons

John Rinzell was away in June 1969
we worked some in July
but Then I had to prepare for ~~Boulder~~
& Oslo.

7/3/69 Rinzell memo summarizing status of spine problem
Asks a number of values & questions.
Spine dimensions, etc.
Some outline for a paper: still optical

7/8/69 My memo for preparation of a short paper.
spine dimensions
specific answers to (7/3/69)

I propose (A) gemmule coupled to
(B) neuron "Greens Fcn"
Suggest simultaneous calc.

7/9/69 New plan ↑ with diagrams
where I state the kinds of solutions needed

This led to John's work collected in hard binder
(7/30/69) Convolution calc.
Solutions of BVP
8/8/69 Convergence tests of series
8/19/69 Summary of Spine Calcs.
which is a shot at a write up
Interrupted by Oslo & Manuscripts for Oslo &
Boulder

November/11/69 New memo on Spines

Nov. 11, 1969

Notes on Dendritic Spines

Re: Strategy to wrap up computations & prepare for publication

Major variables

R_h = spine head membrane resistance

R_{st} = spine stem "

$R_{ds} = R_{ts} = R_{bin}$ input resistance

R_N = whole neuron.

steady state & transient.

Discuss:

(a) degree of isolation

(b) enhanced non-linearity within spine

(c) " linearity between " s

(d) effect of changing R_{st}

Ball park values $R_h \sim 10^9$ to $10^{10}\,\Omega$

$R_{st} \sim 10^7$ to 10^8

$R_{bin} \sim$ { 10^6 to 10^8 for single cyl.; 10^7 to 10^9 for branch location }

(p. 6) predictions

Thoughts about graphs

11/18/69 ~~Solved~~ Wrote soln N cylinders coupled at origin

11/20/69 Wrote solution for one order of branching and generalized to many orders.

12/1/69 What happens when $\Sigma d^{3/2}$ not const. ?

Nov. 11, 1969

Notes on Dendritic Spines

Re: Strategy to wrap up computations & prepare for publication

Major variables

R_b = spine head membrane resistance

R_{st} = spine stem "

$R_s = R_{bs} = R_{bi}$ input resistance

R_N = whole neuron

steady state & transient.

Discuss:

(a) degree of isolation

(b) enhanced non-linearity within spine

(c) " linearity between " "

(d) effect of changing R_{st}

Ballpark values $R_b \sim 10^9$ to $10^{10}\,\Omega$

$R_{st} \sim 10^7$ to 10^8

$R_{bi} \sim \{10^6$ to 10^8 for single cyl.

10^7 to 10^9 for branch location

(p.6) [illegible]

Thoughts about graphs

Write soln.

11/18/69 Solved N cylinders coupled at origin

11/20/69 Wrote solution for one order of branching and generalized to many orders.

12/1/69 What happens when [illegible] ?

12/2/69 Overall BVP for N cylinders
M orders branching

Statement of whole problem
& some intuitive statements

12/3/69 Steady State Diagram
& Hand Calc. St. St. Graph

V_h & V_{BS} vs R_{st}/R_{bin} 10^{-2} to 10^{+2}

for $R_h/R_{bin} = 10$

Worked out image & symmetry approach explicitly, with diagrams, for AAAS - Boston presentation.

12/7/69 I wrote out steady state solutions from superposition
made an error

12/22/69 Rinzell wrote out solutions in Laplace transform form
for cylinders with { sealed end
clamped end

2/3/70 Recap steady state solutions
2/4/70 Begin work on outlines of two papers

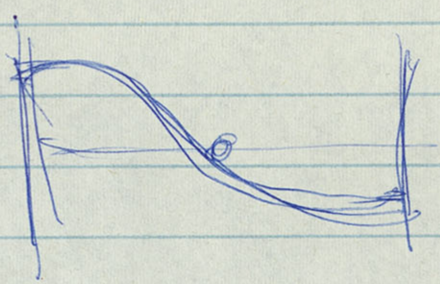
Computed results for current injection
John got results & worked on machine plots

2/10/70 Working outline for papers
2/11/70 ~~Started~~ draft of Section II of Paper A
Steady State Solution for current injection

$$C_0 = \frac{1}{L}\int_0^L F(X)\,dX$$

$$C_1 = \frac{2}{L}\int_0^L F(X)\cos(\pi X/L)\,dX$$

$$\therefore \frac{\left[2\left(\frac{L}{\pi}\right)\sin\left(\frac{\pi X}{L}\right)\right]_A^L}{L-A} = \frac{-2\frac{L}{\pi}\sin(\pi A/L)}{L-A}$$



Peak for Serie

let $n = m$

$$\frac{1}{2}\left[\frac{e^{-Kx}\left(-K\cos 2mx + 2m\frac{\pi}{L}\sin(2mx)\right)}{K^2 + 4m^2\left(\frac{\pi}{L}\right)^2} + \frac{e^{-Kx}(-K+0)}{K^2+0} \right]$$

$0 \to L$

$$\frac{1}{2}\left[\frac{e^{-KL}(-K\cos 2m\pi + 0) + K}{K^2 + 4m^2\left(\frac{\pi}{L}\right)^2} + \frac{-Ke^{-KL} + K}{K^2} \right]$$

$$= \frac{K}{2}\left[\frac{-e^{-KL}+1}{K^2+4m^2\left(\frac{\pi}{L}\right)^2} + \frac{-e^{-KL}+1}{K^2} \right]$$

$$= \frac{K}{2}\left(1-e^{-KL}\right)\left(\frac{2K^2 + 4m^2\left(\frac{\pi}{L}\right)^2}{K^2\left(K^2+4m^2\left(\frac{\pi}{L}\right)^2\right)} \right)$$

$$\frac{K^2 + 2m^2\left(\frac{\pi}{L}\right)^2}{K^2 + 4m^2\left(\frac{\pi}{L}\right)^2}$$

$$\int_0^L e^{-Kx} \cos mx \cos nx \, dx$$

Becau[se] $\cos mx \cos nx = \frac{1}{2}\cos(n+m)x + \frac{1}{2}\cos(n-m)x$

$$\frac{1}{2}\int_0^L e^{-Kx}\cos(n+m)x + e^{-Kx}\cos(n-m)x$$

$$\frac{1}{2}\left[e^{-Kx}\frac{(-K\cos(n+m)x + (n+m)\sin(n+m)x}{K^2+(n+m)^2} + e^{-Kx}\frac{(-K\cos(n-m)x + (n-m)\sin(n-m)x}{K^2+(n-m)^2}\right]_0^L$$

change m to $m\pi x/L$
n to $n\pi x/L$

$$\frac{1}{2}\left(\frac{e^{-KL}\left(-K\cos(n+m)\pi + (n+m)\frac{\pi}{L}\sin(n+m)\pi\right) + K}{K^2+(n+m)^2\left(\frac{\pi}{L}\right)^2} + \frac{e^{-KL}\left(-K\cos(n-m)\pi + 0\right) + K}{K^2+(n-m)^2\left(\frac{\pi}{L}\right)^2}\right)$$

$$\frac{K}{2}\left[\frac{-(-1)^{n+m}e^{-KL}+1}{K^2+(n+m)^2\left(\frac{\pi}{L}\right)^2} + \frac{-(-1)^{n-m}e^{-KL}+1}{K^2+(n-m)^2\left(\frac{\pi}{L}\right)^2}\right]$$

12th CRC Math Table p. 309

Because $\int e^{ax}\cos bx\,dx = \frac{e^{ax}(a\cos bx + b\sin bx)}{a^2+b^2}$

for sin, ~~get~~ ~~cos sin~~ sin − cos

It follows that

$$\int_0^L e^{Kx/2}\left\{\cos n\pi x/L + \frac{KL}{2n\pi}\sin n\pi x/L\right\} =$$

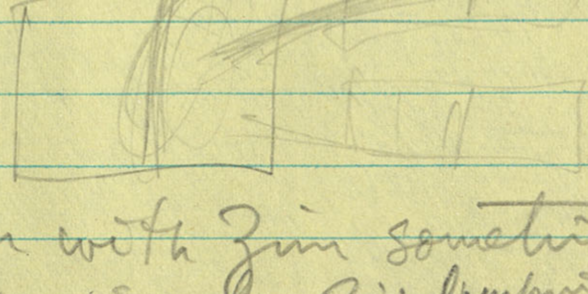
$$\left[\frac{e^{Kx/2}\left(\frac{K}{2}\cos\frac{n\pi x}{L} + \frac{n\pi}{L}\sin\frac{n\pi x}{L}\right)}{\left(\frac{K}{2}\right)^2 + \left(\frac{n\pi}{L}\right)^2} + \frac{e^{Kx/2}\left(\frac{K^2L}{4n\pi}\sin\frac{n\pi x}{L} - \frac{KL}{2n\pi}\left(\frac{n\pi}{L}\right)\cos\right)}{\left(K/2\right)^2 + \left(\frac{n\pi}{L}\right)^2}\right.$$

$$\frac{q\alpha r^2}{c\alpha r}$$

$$\frac{q}{c}\alpha r$$

C_i

g_{ij}



Should sit down with Zim sometime to get correct expression for g_{ij} damping at branch points